

Claims: -

- Sub D1
1. A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) formulation for oral administration, which comprises particles of said SSRI or a pharmaceutically acceptable salt thereof coated with rate-controlling polymer which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.
2. A formulation according to Claim 1, wherein the particles are pellets.
- 10 3. A formulation according to Claim 2, wherein said pellets comprise a core of said SSRI or a pharmaceutically acceptable salt thereof coated with said rate-controlling polymer to form a rate-controlling membrane surrounding said core.
- 15 ~~4. A formulation according to Claim 3, wherein the rate-controlling membrane is made up of a major proportion of a pharmaceutically acceptable film-forming, water-insoluble polymer and optionally a minor proportion of a pharmaceutically acceptable film-forming, water-soluble polymer, <sup>wherein</sup> the ratio of said water-insoluble polymer to said water-soluble polymer, when said water-soluble polymer is present, being effective to permit a SSRI release rate which allows controlled release of SSRI over a period of not less than about 12 hours following oral administration.~~
- 20 5. A formulation according to Claim 4, wherein the rate-controlling membrane contains an ammonio methacrylate co-polymer.
- 12

6. A formulation according to any one of Claims 2-5, wherein the core further comprises an organic acid, the SSRI component and the organic acid being present in a ratio of from 50:1 to 1:50.

5 7. A formulation according to any preceding claim, wherein the SSRI is selected from citalopram, clomipramine, fluoxetine, fluvoxamine, paroxetine, sertraline, trazodone, venlafaxine and zimeldine or a pharmaceutically acceptable salt thereof.

8. A formulation according to Claim 7, wherein the SSRI is fluvoxamine or a pharmaceutically acceptable salt thereof.

10 9. A formulation according to any preceding claim, wherein the SSRI release rate from the particles when measured *in vitro* using a USP type II dissolution apparatus (paddle) according to US Pharmacopoeia XXII in 0.05 M phosphate buffer at pH 6.8 substantially corresponds to the following dissolution pattern:

- 15 (a) No more than 15% of the total SSRI is released after 0.5 of an hour of measurement in said apparatus;
- (b) No more than the 25% of the total of SSRI is released after 1 hour of measurement in said apparatus;
- 20 (c) Between 20% and 75% of the total SSRI is released after 2 hours of measurement in said apparatus;
- (d) Not less than 75% of the total SSRI is released after 4 hours of measurement in said apparatus; and

- (e) Not less than 85% of the total SSRI is released after 6 hours of measurement in said apparatus.

10. A formulation according to any one of Claims 1-8, wherein the the SSRI release rate from the particles when measured *in vitro* using a USP type II dissolution apparatus (paddle) according to US Pharmacopoeia XXII in 0.05 M phosphate buffer at pH 6.8 substantially corresponds to the following dissolution pattern:

- (a) No more than 20% of the total SSRI is released after 4 hours of measurement in said apparatus;
- 10 (b) No more than 45% of the total SSRI is released after 6 hours of measurement in said apparatus;
- (c) Between 45% and 80% of the total SSRI is released after 8 hours of measurement in said apparatus;
- 15 (d) Not less than 70% of the total SSRI is released after 10 hours of measurement in said apparatus; and
- (e) Not less than 80% of the total SSRI is released after 12 hours of measurement in said apparatus.

20 11. A multiparticulate controlled release SSRI formulation according to Claim 1, substantially as hereinbefore described and exemplified.

112

12. A controlled release SSRI formulation for oral administration comprising a blend of particles as defined in any one of Claims 1-11.

5 13. A controlled release SSRI formulation for oral administration comprising a blend of particles as defined in any one of Claims 1-11 in admixture with an immediate release form of SSRI or a pharmaceutically acceptable salt thereof to ensure a rapid attainment of effective therapeutic blood levels.

10 14. A formulation according to Claim 13, wherein the immediate release form of SSRI comprises pellets as defined in any one of Claims 3-11 without said rate-controlling membrane.

15 15. A formulation according to any one of Claims 12-14, wherein the SSRI release rate when measured *in vitro* using a USP type II dissolution apparatus (paddle) according to US Pharmacopoeia XXII in 0.05 M phosphate buffer at pH 6.8 substantially corresponds to the following dissolution pattern:

- (a) No more than 20% of the total SSRI is released after 1 hour of measurement in said apparatus;
- (b) No more than 60% of the total SSRI is released after 2 hours of measurement in said apparatus;
- (c) Not less than 20% of the total SSRI is released after 4 hours of measurement in said apparatus;

(d) Not less than 35% of the total SSRI is released after 6 hours of measurement in said apparatus;

(e) Not less than 50% of the total SSRI is released after 8 hours of measurement in said apparatus;

5 (f) Not less than 70% of the total SSRI is released after 10 hours of measurement in said apparatus; and

(g) Not less than 75% of the total SSRI is released after 12 hours of measurement in said apparatus.

10 16. A formulation according to any one of Claims 12-14, wherein the SSRI release rate when measured *in vitro* using a USP type II dissolution apparatus (paddle) according to US Pharmacopoeia XXII in 0.05 M phosphate buffer at pH 6.8 substantially corresponds to the following dissolution pattern:

15 (a) No more than 20% of the total SSRI is released after 1 hour of measurement in said apparatus;

(b) No more than 45% of the total SSRI is released after 2 hours of measurement in said apparatus;

(c) Between 20% and 70% of the total SSRI is released after 4 hours of measurement in said apparatus;

20 (d) Between 35% and 85% of the total SSRI is released after 6 hours of measurement in said apparatus;

- (e) Not less than 50% of the total SSRI is released after 8 hours of measurement in said apparatus;
- (f) Not less than 70% of the total SSRI is released after 10 hours of measurement in said apparatus; and
- 5 (g) Not less than 75% of the total SSRI is released after 12 hours of measurement in said apparatus.

17. A formulation according to any one of Claims 12-14, wherein the SSRI release rate when measured *in vitro* using a USP type II dissolution apparatus (paddle) according to US Pharmacopoeia XXII  
10 in 0.05 M phosphate buffer at pH 6.8 substantially corresponds to the following dissolution pattern:

- (a) No more than 50 % of the total SSRI is released after 2 hours of measurement in said apparatus;
- (b) Not less than 35% of the total SSRI is released after 6 hours  
15 of measurement in said apparatus; and
- (c) Not less than 80% of the total SSRI is released after 22 hours of measurement in said apparatus.

18. A controlled release SSRI formulation according to Claim 12 for oral administration, substantially as hereinbefore described and  
20 exemplified.

19. A method for the treatment of depression, obsessive compulsive disorder or <sup>15</sup>other condition treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate
- 5 controlled release SSRI formulation according to any one of Claims 1-11 or a controlled reslease SSRI formulation according to any one of Claims 12-18.

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D<sub>1</sub>

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C<sub>1</sub>

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D<sub>2</sub>